

AD-A160 714

THE EFFECTS OF SANGUINARIA EXTRACT ON PLAQUE RETENTION  
AND GINGIVAL HEALTH (U) AIR FORCE INST OF TECH  
WRIGHT-PATTERSON AFB OH R A MILLER 1985  
AFIT/CI/NR-85-1217

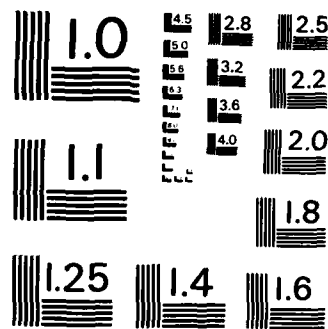
1/1

UNCLASSIFIED

F/G 6/15

NL

			th	th	.I.	.I.				END			
			th	th	.I.	.I.				FILED			
										DTIC			



MICROCOPY RESOLUTION TEST CHART  
NATIONAL BUREAU OF STANDARDS-1963-A

UNCLASS

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER AFIT/CI/NR 85-121T	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) The Effects of Sanguinaria Extract on Plaque Retention and Gingival Health in Active Orthodontic Patients		5. TYPE OF REPORT & PERIOD COVERED THESIS/DISSERTATION
7. AUTHOR(s) Robert A. Miller		6. PERFORMING ORG. REPORT NUMBER
9. PERFORMING ORGANIZATION NAME AND ADDRESS AFIT STUDENT AT: Virginia Commonwealth University		8. CONTRACT OR GRANT NUMBER(s)
11. CONTROLLING OFFICE NAME AND ADDRESS AFIT/NR WPAFB OH 45433 - 6583		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)		12. REPORT DATE 1985
		13. NUMBER OF PAGES 33
		15. SECURITY CLASS. (of this report) UNCLASS
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE
16. DISTRIBUTION STATEMENT (of this Report) APPROVED FOR PUBLIC RELEASE; DISTRIBUTION UNLIMITED		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)		
18. SUPPLEMENTARY NOTES APPROVED FOR PUBLIC RELEASE: IAW AFR 190-1  18 Oct 85 Lynn E. Wolaver Dean for Research and Professional Development AFIT, Wright-Patterson AFB OH		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number)		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) ATTACHED		

AD-A160 714

MIC FILE COPY

DTIC  
ELECTE  
OCT 30 1985  
S E D

DD FORM 1 JAN 73 1473

EDITION OF 1 NOV 65 IS OBSOLETE

UNCLASS

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

## Summary

✓ Controlling plaque accumulation in orthodontic patients is of primary importance to all orthodontists. A new antiplaque chemotherapeutic agent which contains sanguinaria extract has recently been introduced and proven to be effective in periodontal patients. This study tests a .03 per cent sanguinaria chloride mouthrinse and toothpaste in orthodontic patients. A 12 week double blind comparison was done to test the effects of a sanguinaria extract mouthrinse and toothpaste in orthodontic patients. In this study it was reported that the sanguinaria extract active group showed a 53 per cent reduction in the mean plaque index and a 50 per cent reduction in the mean gingival index. This suggests that the mouthrinse and toothpaste containing sanguinaria extract have a benefit in controlling plaque and reducing gingivitis in orthodontic patients.

Accession For	
NTIS GRA&I	<input checked="" type="checkbox"/>
DTIC TAB	<input type="checkbox"/>
Unannounced	<input type="checkbox"/>
Justification	
By	
Distribution/	
Availability Codes	
Dist	Avail and/or Special
A-1	



**The Effects of Sanguinaria Extract on Plaque  
Retention and Gingival Health in  
Active Orthodontic Patients**

**Thesis**

**Submitted for Partial  
Fulfillment of the Requirements for a Certificate  
in Orthodontics at the Medical College of Virginia  
Virginia Commonwealth University**

**By:**

**Robert A. Miller, D.M.D.  
Orthodontic Resident**

**James E. McIver, D.D.S.  
Advisor and Chairman  
Department of Orthodontics**

**Jack C. Gunsolley, D.D.S.  
Periodontal Resident and Statistician**

**85 10 30 003**

## Introduction

Orthodontists are aware of the challenge their patients have in practicing oral hygiene. Due to the presence of bands, brackets and arch wires, these patients must spend more time and use many techniques to obtain adequate plaque removal. Failure to manage plaque removal during orthodontic treatment may lead to early loss of tooth support<sup>2</sup> and an increased incidence of decalcification and carious lesions.<sup>3</sup> Many orthodontists combat the problem of oral hygiene in their patients by first demonstrating a technique of plaque removal that is effective before orthodontic treatment begins. This is followed by positive reinforcement techniques as treatment proceeds.<sup>4</sup>

Within the past 15 years much emphasis has been placed on developing chemotherapeutic antimicrobial agents that can control the plaque in all people. Most of these have been designed to be used on a daily basis. These agents could produce some benefits in orthodontic patients if they were proven to be effective in reducing plaque.

The purpose of this study is to test one of these chemotherapeutic agents in patients undergoing active orthodontic therapy. A double blind clinical trial was carried out to test the hypothesis that a .03 per cent sanguinaria extract mouthrinse and toothpaste are of value in the maintenance of gingival health and plaque control in patients undergoing fixed appliance orthodontic therapy.

### Review of the Literature

The philosophy of dental treatment utilizing chemotherapeutic agents rely on the validity of the specific plaque hypothesis<sup>5</sup> which means that certain forms of dental decay and periodontal disease are due to an overgrowth of certain indigenous bacteria. Investigations in humans have shown that bacteria removed from diseased sites have characteristic microbial profiles that differ from bacteria from non-diseased sites.<sup>5,6</sup> Organisms in supragingival plaque are different from those in subgingival plaque. In general, more gram negative organisms are in subgingival pockets (75 per cent) whereas supragingival plaque consist primarily of gram positive organisms (90 per cent).<sup>6</sup> These percentages differ from one individual to another, and also differ in varying stages of periodontal disease. In general, there is an apparent overgrowth of gram negative organisms in subgingival plaque in gingivitis.<sup>6</sup>

The ideal antiplaque chemotherapeutic agent should help control harmful elements of plaque while encouraging protective species of bacteria to predominate. The main criteria one should use when selecting a chemotherapeutic agent is the spectrum of activity agent against odontopathic flora.<sup>5</sup> There are other properties of chemotherapeutic agents that must be considered. These ideal properties include<sup>7</sup>:

1. safe for intraoral use
2. bacteriacidal against cariogenic and plaque forming organisms
3. retained in the mouth for extended periods of time
4. capable of penetrating dense microbial plaque
5. not alter intestinal flora or be absorbed in the gastrointestinal tract.

One of the more recent antiplaque agents that has been extensively tested is Chlorhexidine. Chlorhexidine, a bisbiguanide chemical compound, has a remarkable ability to reduce plaque and prevent gingivitis<sup>5</sup>. Chlorhexidine gluconate is an effective mouth rinse that is widely used throughout Europe and has recently been approved by the Food and Drug Administration and is expected to be commercially available in the United States by June 1985<sup>8</sup>.

Stirrups et al.<sup>9</sup> studied the effects of Chlorhexidine in 64 subjects during fixed orthodontic therapy for four months. The subjects used 5 ml. of .2% Chlorhexidine gluconate (Corsodyl ICIA) twice a day for a four month period and a placebo during another four month period. The two test periods were separated by a two month recovery period. The two test periods were separated by a two month recovery period. At monthly intervals, assessments were made of both the plaque retention and gingival condition utilizing the 0-3 Plaque and Gingival Index system. This trial showed a statistically significant ( $p < .001$ ) reduction in both the plaque and gingival indices in the active mouthrinse subjects. However, since four months was considered to be a long period of use, the clinical application of Chlorhexidine in orthodontic patients is limited mainly to acute gingival conditions. Also a highly significant incidence of staining ( $p < .001$ ) was observed in the active group of patients which is one of the characteristic side effects of Chlorhexidine. These stains are easily removed at the time of appliance removal but are unacceptable to the patients during treatment. Daily use of Chlorhexidine causes an esthetically displeasing stain on the teeth of patients. There have also been clinical case reports of mucosal desquamitive reactions following daily usage of .2 per cent gluconate Chlorhexidine<sup>10</sup>. In all three cases reported, the range of time in which the mouth rinse was used was two to six months.



Three reasons that were given to account for the desquamitization that occurred in the three reported cases.

1. direct cytotoxicity to the oral mucosa
2. precipitation of the salivary mucin coat which causes the mucosa to crack under stain and normal muscle activity
3. precipitation and inactivation of secretory I A which makes the oral mucosa more susceptible to viral attack

In all three cases, chlorhexidine rinsing was terminated which followed with healing.

Recently, a new antiplaque agent 11,14,15,16 has been introduced that has been proven to be effective in reducing plaque and gingival inflammation and can be administered on a daily basis. This agent utilizes sanguinaria extract, a group of plant alkaloids, as its active ingredient. Sanguinaria is a group of benzophenothridine alkaloids that are extracted from the Sanguinaria canadensis L.<sup>11</sup> or bloodroot plant. Sanguinarine is only one of six major alkaloids and has been found to contribute the most to the sanguinaria extract<sup>11</sup>. Throughout the remainder of this paper, the term Sanguinaria extract will be used to describe the active ingredient unless specified otherwise by another author.

The antiplaque effects of sanguinaria extract are due mainly to its retention in the plaque and inhibition of new plaque formation<sup>11</sup>. In a study conducted at the University of Pennsylvania, 24 subjects participated in a supervised oral rinse experimental gingivitis study<sup>11</sup>. They compared sanguinaria extract (.45 per cent), sanguinaria extract (.03 per cent) combined with zinc chloride. Two morning and afternoon supervised rinses were done along with brushing with a non-fluoridated toothpaste. No other oral hygiene measures were allowed. Plaque scores were taken at day 0 and day 8. The

plaque scores for both sanguinaria extract groups decreased significantly ( $p < .05$ )<sup>11</sup> (21.3 per cent plaque reduction for the sanguinaria extract group with zinc chloride and 19.4 per cent reduction of plaque in the sanguinaria extract group). The plaque scores for the placebo group increased 21.3 per cent. This corresponds to a 40.7 per cent difference in plaque growth between one of the sanguinaria extract groups and the placebo group. The results of this study suggest that a sanguinarine-containing rinse is an important addition to an oral hygiene regimen in achieving an antiplaque benefit above and beyond ordinary toothbrushing and flossing<sup>11</sup>.

The second part of the article reported by Southard<sup>11</sup> tested the retention of sanguinaria in plaque and saliva. Nineteen subjects were instructed to refrain from oral hygiene measures and eating for eight hours. Nine subjects participated in the saliva analysis and ten subjects in the plaque analysis. Sanguinaria extract rinses were given to each subject (15 ml. for 15 seconds) and samples of plaque and saliva were analyzed at different time intervals following the rinse. The results indicated that sanguinarine was present in the plaque at minimum inhibitory concentrations (the concentration at which aerobic and anerobic organisms are inhibited) for up to two hours after rinsing<sup>11</sup>. Saliva levels were found to be maintained for up to 90 minutes<sup>11</sup>.

The article also discusses the fluorescent properties of sanguinarine and how it was used to verify its retention in plaque. Since sanguinarine discloses plaque with the aid of a long-wave ultraviolet light, one can visualize the presence of plaque after rinsing for up to one hour<sup>11</sup>.

Retention of sanguinarine at critical sites of the mouth was also verified by Yankell<sup>12</sup>. He used the saliva glycolysis assay which measures the

inhibition of acid produced in the saliva. In the initial experiment, Yankell compared the antiglycolytic effects of sanguinarine with Chlorhexidine and cetylpyridium chloride (two commercial mouth rinses not yet available in the United States). Sanguinarine was found to have superior antiglycolytic effects at low concentrations (6-12 mg/ml)<sup>12</sup>. At concentrations greater than 12 mg/ml Chlorhexidine was found to have greater antiglycolytic effects<sup>12</sup>. This means sanguinarine is more efficacious at lower concentrations. The minimum inhibitory concentration for sanguinarine (level at which antimicrobial effects are observed) is 8-32 mg/ml<sup>10</sup>. The concentration of the sanguinaria extract has been tested for toxicity and was found to have a lethal dose (LD of 1663.6 mg/kg<sup>11</sup>. This means one would have to consume extremely large quantities of the mouth rinse or toothpaste before any toxic reactions the active ingredient would be observed<sup>8</sup>.

Yankel then compared Viadent<sup>B</sup> to three commercially available mouthrinses. Viadent<sup>B</sup> was more effective in inhibiting salivary glycolysis than Hibitane<sup>D</sup> and Cepecol<sup>E</sup><sup>12</sup>. The final part of this study involved a randomized crossover trial which compared Viadent<sup>B</sup> to a placebo and Listerine<sup>F</sup>. Saliva samples were collected at 15, 45, and 90 minutes. Viadent<sup>B</sup> was found to be superior in inhibiting salivary glycolysis at all times tested<sup>12</sup>. The clinical implications of all three of these experiments are based on the validity that reduced salivary glycolysis is a predictive method of determining if acid producing organisms are being inhibited.

Boulware and Southard<sup>13</sup> studied the ability for the sanguinaria extract to neutralize volatile sulfur compounds which are responsible for oral malodor. A thiol-specific reagent was used to measure levels of reactive sulfur in incubated saliva taken from 8 subjects. The sanguinarine extract, in combination with zinc chloride was found to be more effective than Lavoris<sup>R</sup>, Scope<sup>R</sup>

and Listerine<sup>F</sup> in aggregating thiol substrates which are necessary for bacteria metabolism and are responsible for oral malodor<sup>13</sup>.

The clinical assessment of a combination of Viadent<sup>B</sup> oral rinse and dentrifice for reducing plaque was done by Greenfield and Cachell<sup>14</sup>. They conducted a double blind randomized crossover study that involved sixty adult patients. Half of the patients used the Viadent<sup>B</sup> toothpaste and mouthrinse three times per day. The other half used Zendium<sup>G</sup> toothpaste and tap water mouthrinse. Baseline and two week plaque indices were taken on all of the patients. After a two week wash out period (normal oral hygiene resumed) the subjects crossed over to the other product and baseline and two week plaque indices were taken on each subject. The results indicated a highly significant reduction of plaque ( $p < .001$ ) in those patients who used Viadent<sup>B</sup> (80 per cent improved) as compared with those who used the control product (17 per cent improved). It should be pointed out that the length of this study was short to measure any changes in the gingiva.

To this date there have been no long term studies utilizing sanguinarine extract mouthrinse or toothpaste reported in the literature. Since the lethal dose is high and the minimum inhibitory concentration low, the FDA has currently accepted the Viadent<sup>B</sup> toothpaste and mouthrinse as an esthetic agent which means it can be used on a daily basis<sup>11</sup>.

A study of periodontal therapy patients was done by Oesthby and Persson<sup>15</sup> in which they observed favorable changes in the plaque and gingival indices (an indication of periodontal health).

A 4 week, double blind crossover study was done on 24 patients who used a toothpaste and oral rinse each containing .01 per cent sanguinaria chloride (in combination with zinc chloride and a placebo control. Patients using the

active mouthrinse and toothpaste demonstrated a significant ( $p < .001$ ) improvement in plaque and gingival indices<sup>15</sup>. The lingual surfaces after tested teeth of the active group showed the greatest improvement of plaque and gingival scores when compared to the placebo. During the active test period 79 per cent of the subjects showed an improved plaque index score while 2.1 per cent showed worsened scores. The placebo group showed a 47 per cent improvement of their plaque index scores, while 53 per cent of the subjects showed worsened scores. Gingival index scores showed a similar improvement in the active test group. The active subjects showed a 74 per cent improvement of the gingival index scores while 26 per cent showed worsened scores. During the placebo test period, 47 per cent of the subjects showed an improvement while 53 per cent of the subjects showed worsening of the scores. This study was performed on periodontally compromised patients which may account for some patients with a negative response.

The application of Viadent<sup>B</sup> toothpaste and mouthrinse in Orthodontic patients was first reported by Davidson et al<sup>16</sup>. They described an oral hygiene program that incorporates sanguinaria extract (Viadent<sup>B</sup>) toothpaste and mouthrinse along with sulcus irrigation<sup>16</sup>. On the patients' first visit sulcular brushing techniques are demonstrated and Viadent<sup>B</sup> toothpaste and mouthrinse are introduced. Also dietary counseling is performed. The patients are given an instruction sheet explaining when to brush and floss after each meal. On the second visit, flossing techniques are introduced and a review of brushing is reinforced. The Pro Pulse<sup>B</sup> Irrigation device is demonstrated on the third visit. A .15 per cent sanguinaria extract is the recommended solution to be used in the Pro Pulse<sup>B</sup> prior to bedtime. Also brushing and flossing techniques are reviewed. On the the fourth visit all of the above techniques are demonstrated by the patient. Correction of errors in

technique are made at this appointment. The oral hygiene program used in this practice appears to be organized and effective. Patient education is, however, dependent on properly trained and motivated staff. In conclusion, the main advantages of using a sanguinaria extract mouthrinse and toothpaste by orthodontic patients are:

1. It maintains a high salivary PH which correlates with antiplaque activity for approximately two hours<sup>12</sup>.
2. It inhibits most oral aerobic and anaerobic microorganisms at 8-32 ug/ml (which is maintained for up to two hours)<sup>11</sup>.
3. Sanguinaria extract is safe for daily use.
4. It neutralizes volatile sulfur compounds which are necessary for bacterial growth and oral malodor<sup>13</sup>.

#### Materials and Methods

This study was a four month, double blind randomized study involving fifty (50) orthodontic patients. There were two test materials and two placebo materials. The oral rinse test materials contain 300 mg/ml of Sanguinaria extract and conforms to the formula of Appendix 1. The placebo oral rinse conforms to the formula of Appendix 2. The dentrifice test material contains 750 mg/ml of sanguinaria extract and conforms to the formula of Appendix 3. The dentrifice placebo control conforms to the formula of Appendix 4. The toothbrush prescribed was an Oral B 40 toothbrush.

#### Selection of Treatment Groups

Inclusion Criteria:

1. active orthodontic patients treated at MCV

2. Ten years or older
3. must agree to use only the oral rinse, toothpaste, and toothbrush provided by the investigator and to follow the oral care program as outlined
4. must have no less than 24 teeth, excluding the third molars, on which all tested teeth are either banded or bonded.
5. pocket depth less than 5 mm

Exclusion Criteria:

1. concomitant use of antibiotics
2. concomitant use of prescription anti-inflammatory drugs
3. use of antibiotics within two months of starting the study
4. acute illness
5. diabetes
6. pregnancy
7. any known sensitivity or reaction to: dentrifices, oral rinses, any ingredient appearing in Appendix 1-4
8. any known soft or hard tissue pathology that may affect the health of the patient

Patients meeting all of the inclusion criteria and none of the exclusions were randomly assigned to one of two groups. One group used the test mouth rinse and test toothpaste and the other group used the placebo toothpaste and placebo mouth rinse. The products were labeled and patient numbers were applied by employees of Vipont Laboratories. Eligible patients were assigned numbers in consecutive order, ie. the first patient was patient number 1; the second was patient number 2, etc.

## Study Procedure

Each potential study participant must be an active orthodontic patient with bands and/or bonds on all teeth in both arches (excluding second molars). The study was explained and the consent form reviewed and signed by all interested patients. For each subject the following procedures were performed: a thorough prophylaxis after an initial plaque and gingival index, oral hygiene instructions were reviewed including a review of toothbrushing technique. The following information was recorded on a study report form:

Gingivitis will be evaluated by the Gingival Index (GI) described by Loe<sup>17</sup>.

- 0 = Absence of inflammation, normal gingiva
- 1 = Mild inflammation - slight change in color and little change in texture, no bleeding on probing
- 2 = Moderate inflammation - moderate glazing, redness, edema and hypertrophy. Bleeding on pressure.
- 3 = Severe inflammation - marked redness and hypertrophy. Tendency to spontaneous bleeding. Ulceration.

Plaque will be scored by the method described by Loe<sup>17</sup>.

- 0 = No plaque
- 1 = A film of plaque adhering to the free gingival margin and adjacent areas of the tooth. The plaque may be seen in situ only after application of disclosing solution or by using the probe on the tooth surface.
- 2 = Moderate accumulation of soft deposits within the gingival pocket, or on the tooth and gingival margin which can be seen with the naked eye.



3 = Abundance of soft matter within the gingival pocket and/or on the tooth and gingival margin.

\* The six Ramjford<sup>18</sup> teeth were chosen for partial mouth indices. They include  $\frac{6}{4,1} \mid \frac{14}{6}$ . The alternate teeth are  $\frac{4,1}{6} \mid \frac{6}{1,4}$ .

Since one clinician performed all of the plaque and gingival indices, standardization of the scoring technique is for consistency of scoring from day to day. The technique for standardization included five patients. PI and GI scores was performed utilizing the scoring criteria described in the preceding paragraph. Following at least a fifteen minute time interval, a second score was taken and compared to the first. The investigator was considered standardized when 80 per cent agreement was obtained for the reported tests of PI and GI.

#### Baseline Phase of Treatment

Two clinical examinations were performed prior to the experimental phase to establish a plaque and gingival index baseline. The first baseline clinic exam (Visit 1) occurred at Day 0. A plaque and gingival index was taken prior to the prophylaxis that was also performed on that day. The Bass technique<sup>16</sup>, a toothbrushing method, was prescribed in this study. The following statements were made to all of the patients:

1. Use a sulcular brushing pattern, then brush in the direction that the teeth grow.
2. Brush two teeth at a time.
3. Develop a pattern (start to finish) so all surfaces are covered.
4. Brush above and below the braces.
5. Brush at least twice a day, once in the morning, after breakfast, and at night before retiring in the evening.

A non-fluoridated toothpaste was used during the first month of the study which eliminates a variable that would affect the results during the experimental phase.

The second baseline clinical exam (Visit 2) occurred in 3 weeks. A plaque and gingival index was recorded prior to the application of the experimental agents which started on that day. A second prophylaxis was performed at Visit 2. The reason for this was to reduce the amount of established plaque. All patients were asked to demonstrate the oral hygiene technique that was taught to them at their previous appointment. Oral hygiene instructions were reinforced when necessary.

### Experimental Phase of Treatment

Enrolled subjects were instructed to use only the oral rinse, toothpaste and toothbrushes provided. The subjects were instructed to follow the normal oral hygiene practice that they learned at Visits 1 and 2. Patients were instructed not to use dental floss. Clinical evaluation of the experimental phase began at Visit 3 (6 weeks). At each visit the inclusion/exclusion check list was updated and a plaque and gingival index was taken. At each visit data was recorded without reference to any previous visit.

Visit 1 (day 0)	Clinical evaluation/prophylaxis including oral hygiene instructions
Visit 2 (3 weeks)	Clinical evaluation/PI/GI/initiate experimental phase, prophylaxis including oral hygiene instructions, if necessary.
Visit 3 (6 weeks)	Clinical evaluation/PI/GI
Visit 4 (9 weeks)	Clinical evaluation/PI/GI
Visit 5 (12 weeks)	Clinical evaluation/PI/GI,

### Dosage and Duration of Treatment

Patients used the assigned dentrifies and oral rinses twice daily. The patients used a single ribbon of dentrifice on the toothbrush for a period of two minutes for brushing in the morning and before retiring in the evening. Subjects were provided with two identical toothbrushes and encouraged to label the toothbrushes (1 for morning, 1 for night) so they always had a dry toothbrush. The oral rinse was used in the morning and before retiring after brushing. During the use of the oral rinse, two consecutive 15 second rinses

of 15 ml. (1 cap full) each were used. After expelling the second 15 ml. rinse, the subjects were asked not to rinse with water.

#### Monitoring for Adverse Experiences

Any adverse effects, reported by the patient or observed by the investigator, will terminate the patient's role in the study. All patient reports of stinging, burning, irritation, etc. will be recorded on the case report forms. All changes noted during the oral cavity examinations will be recorded on the case report forms. The investigator will record his opinion of the relationship of the study materials to each adverse experience and/or change in the oral cavity. Any serious adverse experience or suspected allergic response will be photographed and reported to the sponsor.

#### Criteria for Discontinuing Use of the Control or Study Material

Patients will be discontinued from the study if any of the exclusion criteria events occur. If, in the investigator's opinion, the subject is no longer an appropriate study participant, the subject may be removed from the study and the reason recorded on the case report form. The subject can also choose to leave the study.

After three months use of the mouthrinse and toothpaste, the following questions were asked:

1. Does the use of a sanguinaria mouthrinse and toothpaste after 9 weeks in orthodontic patients cause a significant reduction of plaque and/or a reduction in the gingival indices (indicating better gingival health)?
2. Are the changes in plaque and gingival index changes seen in non-orthodontic patients reported by Greenfield<sup>14</sup> and Oestby<sup>15</sup> also observed in orthodontic patients?
3. Is the taste acceptable to orthodontic patients?

## Analysis and Results

The data used in this study was obtained from 22 (16 female and 6 male) active ingredient patients and 18 (15 female and 3 male) control ingredient patients. The range in age for all patients is 10-35. A total of 5440 plaque and gingival index values were obtained from 40 patients over the twelve week test period. Ten subjects left the study for various reasons. Two patients had to be removed due to the use of antibiotics during the test period. One patient was eliminated because his bands and bonds were removed during the test period. Four patients were eliminated due to problems with appointments. If a patient missed an appointment and was not rescheduled within two weeks they were eliminated. The remaining three patients were eliminated because they did not like the taste of their toothpaste and mouthwash (one placebo and two active ingredient patients).

Similarities among the two study groups were analyzed for differences in sex, age, initial plaque and gingival indices. A sex chi square test was used to test the similarities among groups due to sex differences. A chi square value of .639 with one degree of freedom indicates no significant difference ( $p=.424$ ) between the two groups due to sex differences. A one way analysis of variance was used to test the differences between the two groups due to age. There were no significant differences ( $p=.85$ ) between the two test groups due to differences in age. There were also no significant differences found between the groups due to the initial gingival index ( $p>.05$ ) and the initial plaque index ( $p>.05$ ).

The statistical model used for the analysis of the plaque index and gingival index over time was the univariate approach to analysis of means. A mixed model, one-way analysis of variance was used to test the difference in

means of the indices. This test is used to see if significant changes within each group are observed over time. Tukey's test for multiple comparisons was used to test the differences between time/group points. This test is used to see if significant changes are observed between the active and placebo groups at specific time intervals with a correction for multiple comparisons.

There were no significant differences between the two groups in the initial mean plaque index (Fig. 1). The placebo group did not significantly change from that time on. The mean plaque index initially was .9 and after 12 weeks it was reduced to .7 which was a 22 per cent reduction of plaque (Fig. 1) which is not statistically significant. The active group had a significant decrease ( $p < .05$ ) week 3 to week 6 and then stayed significantly less than the placebo group ( $p < .05$ ). The overall mean plaque index for the active group went from .95 initially to .45 (after 12 weeks) which is 53 per cent reduction in plaque (Fig. 1).

The means of the gingival index of the two groups initially did not differ significantly (Fig. 2). After oral hygiene instructions (week 0) both increased by the 3 week period but only the placebo increased significantly ( $p < .05$ ). During the experimental period the active group had gradual decreases that were significantly less than the placebo group ( $p < .05$ ) at each visit from week 6 through week 12 (Fig. 2). There was an overall 6 per cent mean gingival index reduction in the placebo group and a 50 per cent mean gingival index reduction in the active ingredient group (Fig. 2).

In Figure 3 and 4 the number of plaque and gingival index scores observed initially and at 12 weeks in the active and placebo groups are bar grafted. A description of these results will be made followed by the clinical implications.

The number of plaque index scores of two were reduced in the placebo group (105-47) but more in the active group (132-10), (Fig. 3). The plaque index scores of one decreased in the active group (222-194) and increased in the placebo group (178-197) (Fig. 3). The plaque index score of zero increased in the active group (168-324) and slightly increased in the placebo group (148-187) .

The gingival index changes for the active and placebo groups were synonymous to changes observed among the plaque indices. Only one gingival index score of three was recorded for each active and placebo group on the first visit. The placebo group had one three at the end of the study and the active group had none. There were not enough gingival index scores of three to make any inferences. The number of gingival index scores of two decreased in the active group (59-11) and decreased slightly in the placebo group (52-50) (Fig. 4). The number of gingival index scores of one decreased in the active group (365-233) and they decreased slightly in the placebo group (283) (Fig. 4). The number of gingival index scores of zero increased in the active group (103-284) and slightly increased in the placebo group (94-98) (Fig. 4).

The changes observed in the individual plaque and gingival index scores indicate that motivation plays an important role to reduce scores of three and two in both the active and placebo groups. The reduction of the plaque and gingival index score to one and zero in the active group must be due to the active ingredient along with adequate oral hygiene technique.

## DISCUSSION

Reduction of plaque and gingival indices seen in orthodontic patients suggests that a sanguinaria extract mouthwash and toothpaste have both a preventive and therapeutic effect. A 54 percent reduction in the mean plaque index and a 50 percent reduction in the mean gingival index was observed in the active group of orthodontic patients. Oestby and Persson<sup>15</sup> conducted a similar study on patients undergoing periodontal therapy. They found a 79 percent reduction in the mean plaque index and a 74 percent reduction in the mean gingival index. In another similar study by Greenfield and Cuchel<sup>14</sup> similar results were obtained. They found an 80 percent mean plaque index reduction in the active group of patients and a 17 percent reduction in the placebo group of patients. In conclusion, the observations reported by Oestby and Peerson<sup>15</sup> and Greenfield and Cuchel<sup>14</sup> were also observed in orthodontic patients.

Some clinical observations were noted during the study that should be discussed. From the first to the second visit (3 weeks), the mean plaque index decreased in both the active and placebo group by 31 percent (Figure 1). The mean gingival index for both groups increased over the same period by 10 percent (Figure 2). The reason for this may be due to an initial increase in over-zealous oral hygiene procedures performed by the patient which traumatized the gingiva. After the administration of the active ingredient and placebo mouthrinse and toothpaste both the mean plaque and gingival index began to diverge over time (Figure 1 and 2). Since the mean plaque and gingival indices for the active group decreased significantly ( $p < .05$ ) the use of Sanguinaria extract mouthwash and toothpaste was found to be beneficial.



The taste of the active ingredient mouthrinse and toothpaste was unacceptable by 2 out of 22 active patients. This appeared to be an initial problem with many others but after the initial 3 week test period most had accepted the unique bitter flavor and some patients actually like the way it tastes.

In conclusion, the sanguinaria extract mouthrinse and toothpaste are recommended in addition to normal oral hygiene procedures described by Davidson and Swanborn<sup>16</sup>. The more time and effort these patients put into oral hygiene procedures, the more likely they will maintain the health of the gingiva throughout treatment. It is my recommendation that these patients be monitored periodically (once every 3 months) by the orthodontist for oral hygiene progress using the partial recording indices described by Loe<sup>17</sup>. This will allow the orthodontist to evaluate the progress each patient is making with his or her oral hygiene and is relatively easy to perform. It is clear that motivation is still an important factor necessary in all oral hygiene programs. If, however, a Sanguinaria extract mouthrinse and toothpaste is used in conjunction with good brushing, flossing, and oral irrigation, orthodontic patients can maintain better gingival health throughout fixed appliance therapy.

# APPENDIX 1

Deionized Water	82.250
Zinc Chloride, USP	0.200
Glycerin	3.500
Sodium Saccharin, USP	0.100
SDA 38F Alcohol	10.143
Poloxamer 407	0.100
Polysorbate 80	0.500
Flavor	0.207
Vipont Fluid Extract	<u>3.000</u>
	100.000

## APPENDIX 2

Deionized Water	82.250
Zinc Chloride, USP	0.200
Glycerin	3.500
Sodium Saccharin	0.100
SDA 38F Alcohol	10.143
Poloxamer 407	0.100
Polysorbate 80	0.500
Flavor	0.207
Placebo Fluid Extract	<u>3.000</u>
	100.000

# APPENDIX 3

Glycerin	15.24%
Viscarin TP4	1.20
Sorbitol	19.00
Deionized Water	4.11
Zinc Chloride	2.70
Sodium Saccharin	.30
Dicalcium Phosphate Dihydrous	37.00
Dicalcium Phosphate Anhydrous	6.00
Titanium Dioxide	3.00
Methylparaben	0.15
Propylparaben	0.05
Sodium Lauryl Sufate	1.25
Tween 80	1.50
Fluid Extract	7.50
Flavor	<u>1.00</u>
	<u>100.00</u>

#### APPENDIX 4

Glycerin	15.24%
Viscarin TP4	1.20
Sorbitol	19.00
Deionized Water	4.11
Zinc Chloride	2.70
Sodium Saccharin	0.30
Dicalcium Phosphate Dihydrous	37.00
Dicalcium Phosphate Anhydrous	6.00
Titanium Dioxide	3.00
Methylparaben	0.15
Propylparaben	0.05
Sodium Lauryl Sulfate	1.25
Tween 80	1.50
Placebo Fluid Extract	7.50
Flavor	<u>1.00</u>
	<u>100.00</u>

FIGURE 1

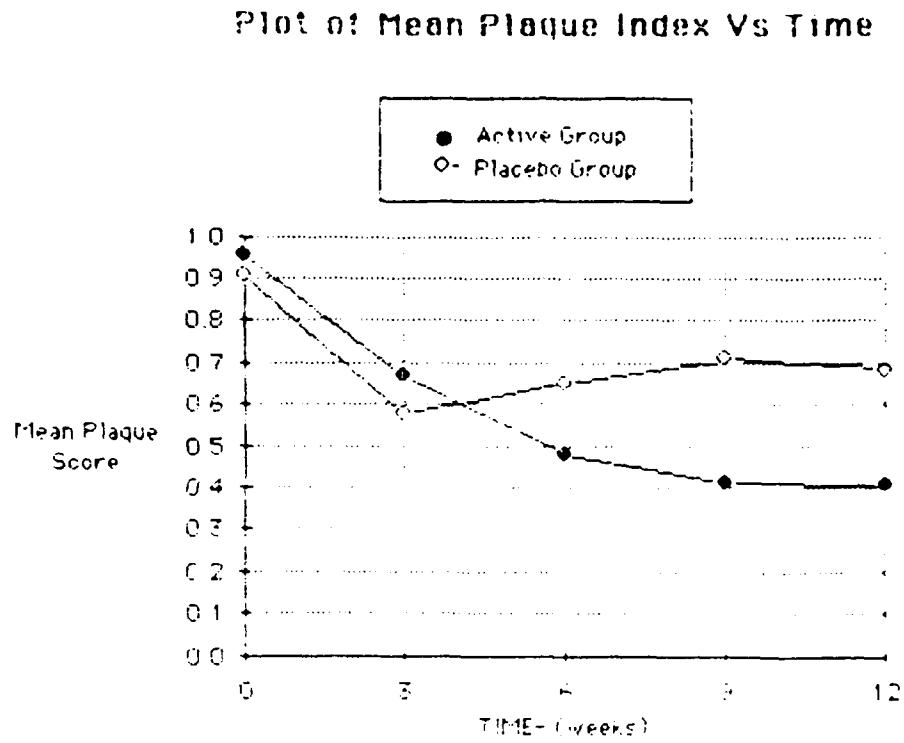


FIGURE 2

### Plot of Mean Gingival Index Vs Time

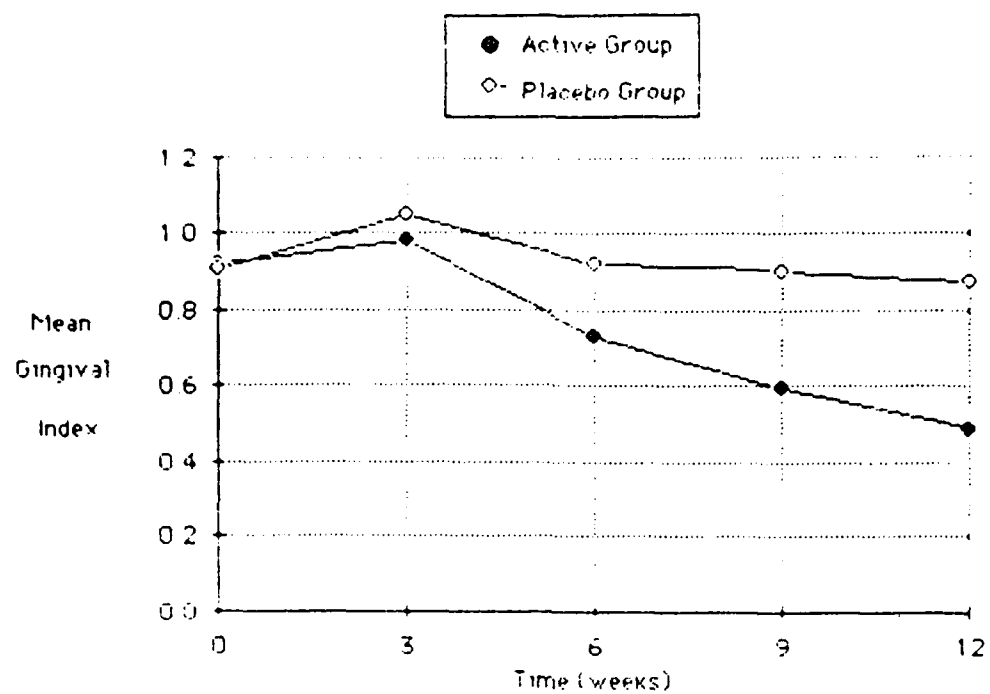


FIGURE 3

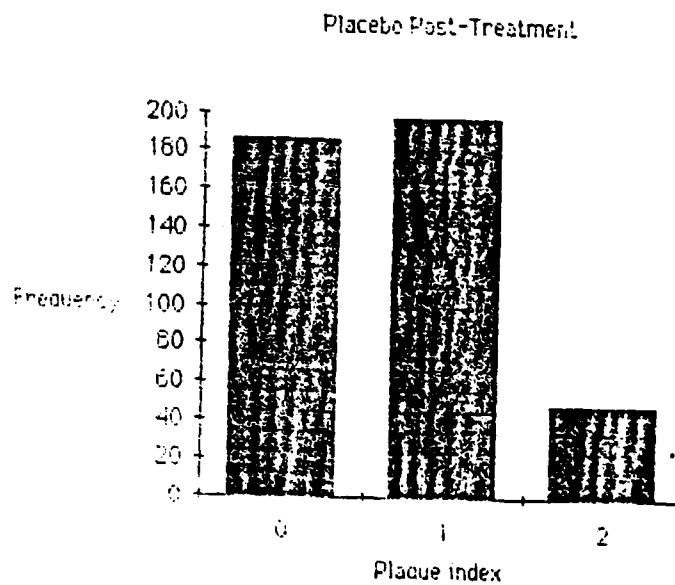
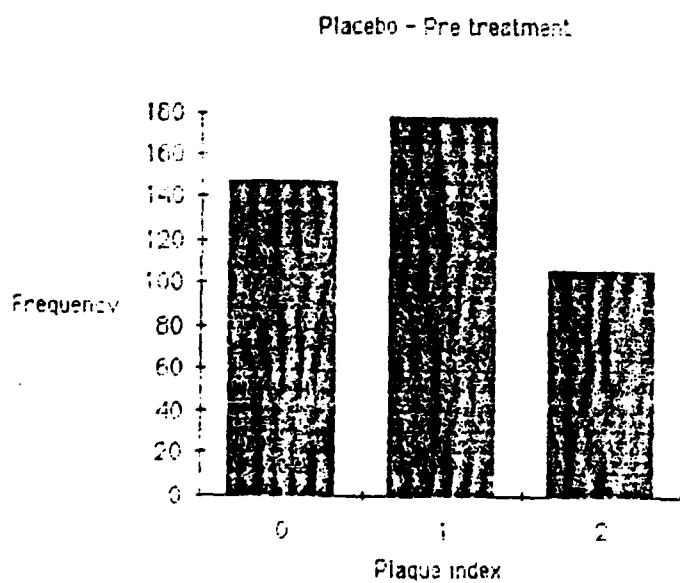
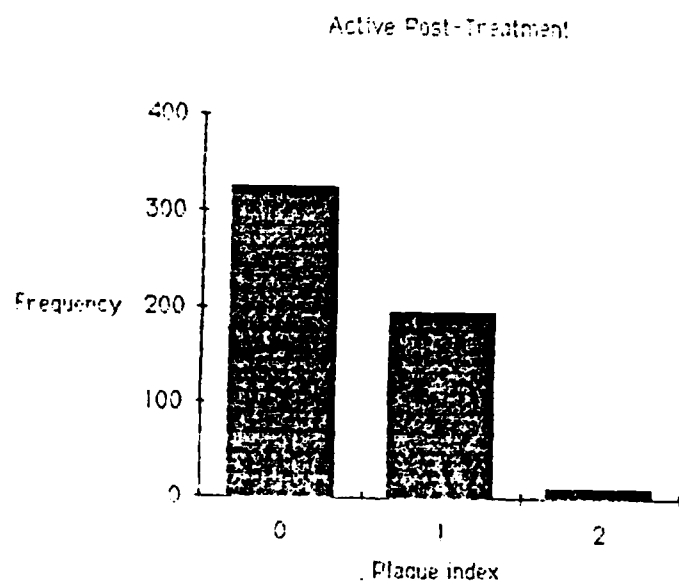
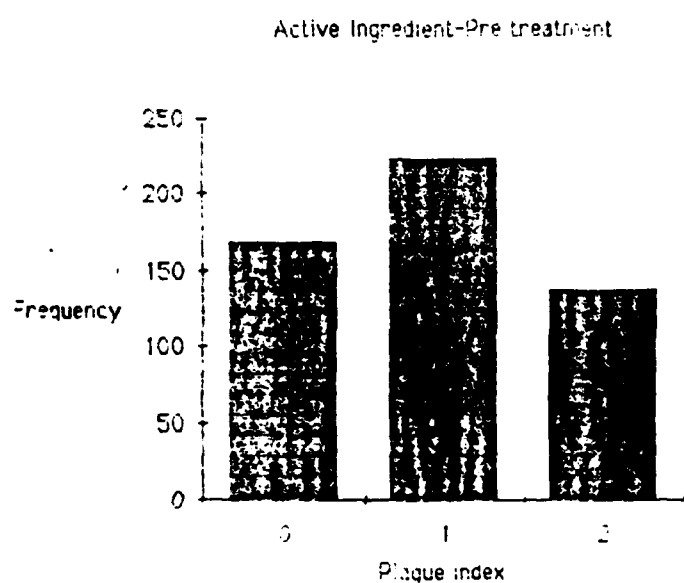
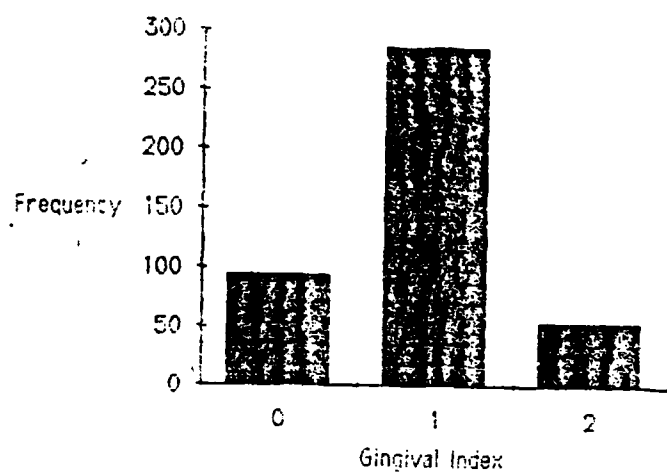


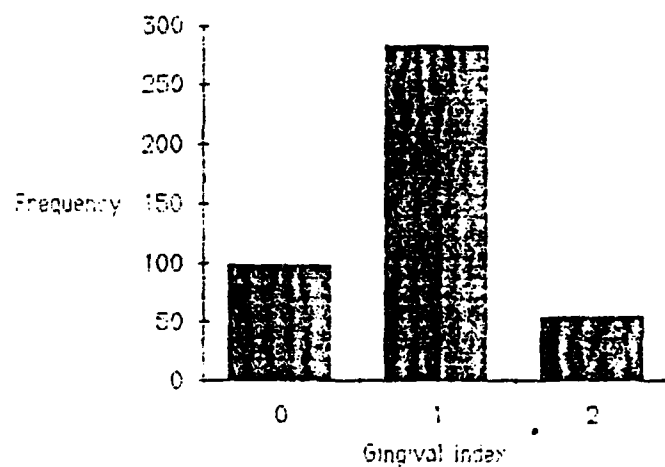


FIGURE 4

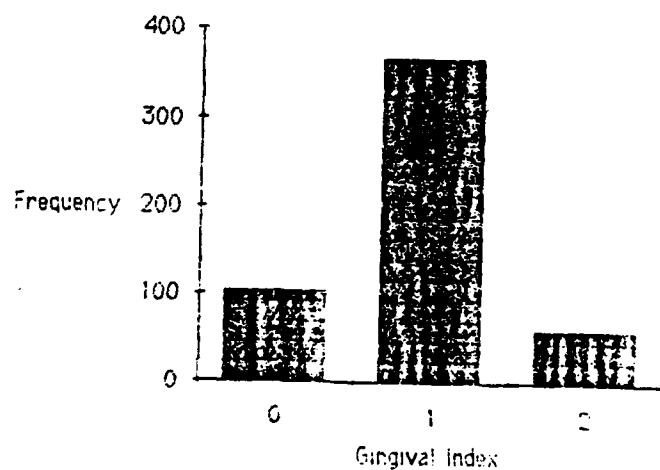
Placebo Pre-treatment



Placebo Post-Treatment



Active Pre-treatment



Active Post-Treatment

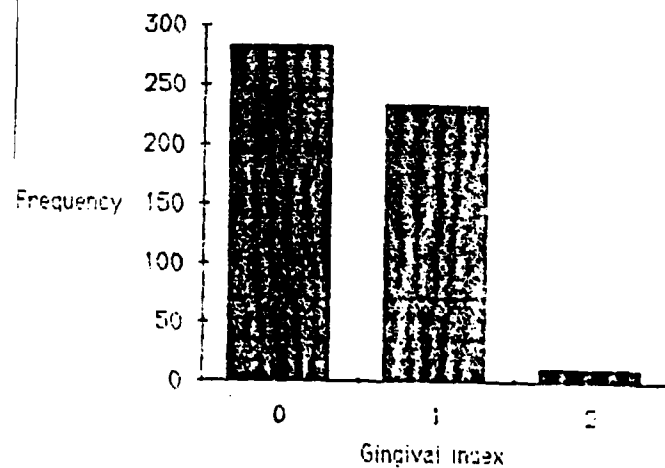


Figure 5

Data Table

Plaque Index

Group

Time	Active				Placebo			
	Plaque Index							
	0	1	2	3	0	1	2	3
1	168	222	132	6	148	178	105	1
2	238	229	60	1	227	162	43	
3	306	190	32		199	185	48	
4	325	187	16		174	210	48	
5	324	194	10		187	197	47	

Gingival Index								
1	103	365	59	1	94	285	52	1
2	60	419	47	2	35	339	58	
3	174	323	31		94	279	59	
4	235	274	19		94	288	48	2
5	284	233	11		98	283	50	1

## References

1. Zachrisson B.U. Oral Hygiene for Orthodontic patients: Current Concepts and Practical Advice. Am. J. Orthod. 66: 487-497. 1974
2. Zachrisson B.U. and Alnaes, L. Periodontal Condition in Orthodontically Treated and Untreated Individuals I., Angle Orthod. 43:402-412, 1973.
3. Zachrisson, B.U. and Zachrisson, S. Carie Incidence and Oral Hygiene During Orthodontic Treatment. Scand. J. Dent. Res. 79:394-401, 1971.
4. Alexander, C.M., Jacobs, J.D., Turpin, D.L.: Disease Control in an Orthodontic Practice, Am. J. Orthod., 71:79-93, 1973.
5. Loesche, W.J., Clinical and Microbiological Aspects of Chemotherapeutic Agents Used According to the Specific Plaque Hypothesis, J. Dent. Res. (58)#12, p. 2404-2412, 1979.
6. S.S. Scoransky, Microbiology of Plaque. The Compendium of Continuing Education in Dentistry Suppl. 5:S53-S56, 1984.
7. Personal Communication with Dr. Dominick Zero, D.D.S., MCV/VCU School of Dentistry.
8. Hamlin Barnes, Associate with Vipont Laboratories.
9. Stirrups, D.R., Laws, E.A., Honigman, J. L., The Effect of a Chlorhexidine Gluconate Mouthrinse on Oral Health During Fixed Appliance Orthodontic Treatment. Brit. Dent. J., 151, #84 . p85-87, 1981.
10. Skoglund, L.A.; Holt, E., Desquamative Mucosal Reactions Due to Chlorhexidine Gluconate. Int. J. Oral Surg. 11(6), 380-2, 1982.
11. Southard, G. L. et al. Sanguinarine, A new antiplaque agent: Retention and Plaque Specificity. J. Amer. Dent. Assoc., #108 pp. 338-341, 1984.
12. Yankell, S.L. Saliva Glycolysis and Plaque. The compendium of continuing education in Dentistry Suppl. 5:S57-S60, 1984.
13. Boulware, R.T., Southard, G.L. Sanguinarine in the control of Volatile

Sulfur compounds in the mouth: A Comparative Study. The Compendium of Continuing Education in Dentistry. Suppl. 5:S61-S64, 1984.

14. Greenfield, W., Cuchel, S.J., The Use of an Oral Rinse and Dentrifice as a System for Reducing Dental Plaque. The Compendium of Continuing Education in Dentistry. Suppl. 5:S82-S86, 1984.
15. Oestby, P.N., Persson, I., Evaluation of Sanguinarine Chloride in Control of Plaque in the Dental Practice. The Compendium of Continuing Education in Dentistry, Suppl. 5:S90-S93, 1984.
16. Davidson, C.O., Swanborn, D.D., Eggleston, D.K., New Anti plaque Agent for Orthodontic Patients, J Clinical Ortho pp. 205-212, Vol. XIX #3, March, 1985.
17. Loe, H. The Gingival Index, the Plaque Index and the Retention Index Systems, J. Periodontol. Vol. 38, 610 - 618, 1967.
18. Ramjford, S.P., Indices for Prevalence and incidence of periodontal disease., J. Periodontol 30:51-59, 1959.

### Product References

- A. Corsodyl, ICI Pharmaceuticals Ltd., Alderly Edge, Cheshire, England.
- B. Vipont Laboratories, Fort Collins Co80524
- C. Vicks Oral Health Group, Richardson-Vicks, Inc. Wilton Ct. 06897
- D. Imperial Chemical Industries Limited Macclesfield, England
- E. Merrel Dow Pharmaceuticals Inc., Cincinnati, OH 45215
- F. Warner-Lambert Co. Morris Plains, NY 07950
- G. Cooper Care Inc. Palo Alto, Ca., 94304

**END**

**FILMED**

**12-85**

**DTIC**